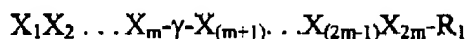


Atty. Dkt. No. 025098-0701

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Presently amended) A method for designing a specific polyamide



wherein

$X_1$ ,  $X_2$ ,  $X_m$ ,  $X_{(m+1)}$ ,  $X_{(2m-1)}$ , and  $X_{2m}$  are carboxamide residues forming carboxamide binding pairs  $X_1/X_{2m}$ ,  $X_2/X_{(2m-1)}$ ,  $X_m/X_{(m+1)}$ ,

$\gamma$  is  $\gamma$ -aminobutyric acid or 2,4 diaminobutyric acid, and

$R_1$  is  $-\text{NH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ ,  $-\text{NH}(\text{CH}_2)_{0-12}\text{CONH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ , or  $-\text{NHR}_2$ , where  $R_2$  and  $R_3$  are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl,  $\text{C}_{1-100}$  alkyl,  $\text{C}_{1-100}$  alkylamine,  $\text{C}_{1-100}$  alkyldiamine,  $\text{C}_{1-100}$  alkylcarboxylate,  $\text{C}_{1-100}$  alkenyl, a  $\text{C}_{1-100}$  alkynyl, and  $\text{C}_{1-100}$  alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL- $\alpha$ -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- $\alpha$ -tocopheral, suitable for use as a DNA-binding ligand that is selective for identified target DNA-sequences  $5'-\text{WN}_1\text{N}_2 \dots \text{N}_m\text{W}-3'$  where m is an integer having a value from 3 to 6, the method comprising:

Atty. Dkt. No. 025098-0701

- (a) identifying a target sequence of double stranded DNA having the form  $5'-WN_1N_2 \dots N_mW-3'$ ,  $N_1N_2 \dots N_m$  being the sequence to be bound by carboxamide residues, wherein each N is independently chosen from the group A, G, C, and T, each W is independently chosen from the group A and T, and m is an integer having a value from 3 to 6;
- (b) representing the identified sequence as  $5'-Wab \dots xW-3'$ , wherein  $a$  is a first nucleotide to be bound by the  $X_1$  carboxamide residue,  $b$  is a second nucleotide to be bound by the  $X_2$  carboxamide residue, and  $x$  is the corresponding nucleotide to be bound by the  $X_m$  carboxamide residue;
- (c) defining  $a$  as A, G, C, or T to correspond to the first nucleotide to be bound by a carboxamide residue in the identified sequence;
- (d) selecting Im as the  $X_1$  carboxamide residue and Py as the  $X_{2m}$  carboxamide residue if  $a = G$ ;
- (e) selecting Py as the  $X_1$  carboxamide residue and Im as the  $X_{2m}$  carboxamide residue if  $a = C$ ;
- (f) selecting Hp as the  $X_1$  carboxamide residue and Py as the  $X_{2m}$  carboxamide residue if  $a = T$ ;
- (g) selecting Py as the  $X_1$  carboxamide residue and Hp as the  $X_{2m}$  carboxamide residue if  $a = A$ ; and
- (h) repeating steps c – g for  $b$  through  $x$  until all carboxamide residues are selected;

Atty. Dkt. No. 025098-0701

wherein Im is N-methylimidazole, Hp is 3-hydroxy-N-methylpyrrole, Py is N-methylpyrrole, A is adenine, G is guanine, C is cytosine, and T is thymine; and;

synthesizing the polyamide.

2. (Cancelled)

3. (Presently amended) The method of claim 2 1 further comprising the step of determining if the binding affinity of the polyamide to the identified target sequence is subnanomolar.

4. (Previously presented) The method of claim 1 further comprising the step of determining if the polyamide exhibits a binding affinity that is at least ten-fold higher for said identified target sequence compared to a non-target DNA sequence.

5. (Presently amended) The method of claim 2 1 further comprising the step of replacing at least one pyrrole residue with a  $\beta$ -alanine residue.

38. (Presently amended) A polyamide composition produced by the method of claim 2 1 wherein one carboxamide binding pair is  $\beta/\beta$ , wherein  $\beta$  is  $\beta$ -alanine.

42. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a regulatory sequence.

43. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a promoter sequence.

Atty. Dkt. No. 025098-0701

44. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a coding sequence.

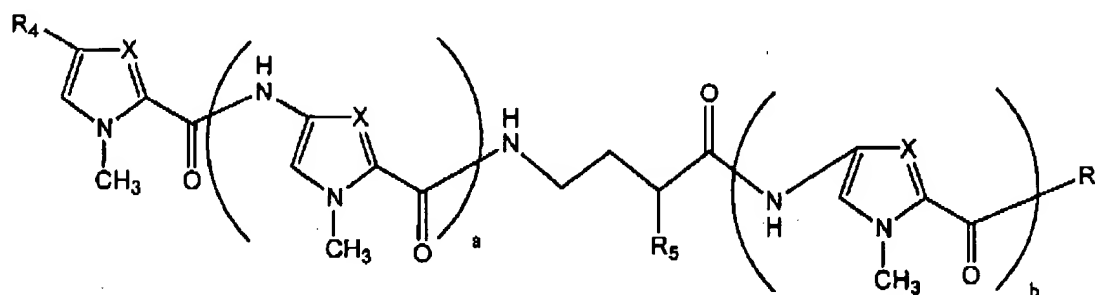
45. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a non-coding sequence.

46. (Presently amended) A polyamide composition produced by the method of claim 2 1 wherein the binding of the carboxamide binding pairs to the identified target DNA sequence modulates the expression of a gene.

47. (Presently amended) A composition comprising an effective amount of a polyamide produced by the method of claim 2 1 and a pharmacologically suitable excipient.

48. (Presently amended) A diagnostic kit comprising a polyamide produced by the method of claim 2 1.

49. (Previously presented) A polyamide designed by the method of claim 1, having the structure:



wherein

Atty. Dkt. No. 025098-0701

$R_4$  is selected from the group consisting of H,  $\text{NH}_2$ , SH, Cl, Br, F, N-acetyl, and N-formyl;

$R_5$  is H or  $\text{NH}_2$ ;

$R_1$  is  $-\text{NH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ ,  $-\text{NH}(\text{CH}_2)_{0-12}\text{CONH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ , or  $-\text{NHR}_2$ , where  $R_2$  and  $R_3$  are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl,  $\text{C}_{1-100}$  alkyl,  $\text{C}_{1-100}$  alkylamine,  $\text{C}_{1-100}$  alkyldiamine,  $\text{C}_{1-100}$  alkylcarboxylate,  $\text{C}_{1-100}$  alkenyl, a  $\text{C}_{1-100}$  alkynyl, and  $\text{C}_{1-100}$  alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL- $\alpha$ -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- $\alpha$ -tocopheral;

each X is independently selected from the group consisting of N, CH, and COH;

each a is an integer from 2 to 5; and

each b is an integer from 3 to 6.